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Dear Editor,

In a recent study 130 pediatric patients were selected according to the following inclusion criteria: diagnosis of epilepsy within the previous 6 months; IQ within normal or borderline range (IQ > 70); no progressive neurological conditions not directly associated with symptomatic epilepsy. The sample considered for follow-up analysis at 18-month follow-up consisted of 40 cases (a per protocol analysis was conducted). The follow-up revealed that about 90% of patients experienced a reduction in both frequency and duration of their seizures with minimal changes in term of drug therapy. On the other hand, their psychopathological assessment pointed to a prevalence of problems, classifiable as anxiety disorders, depressive disorders, and attention deficit hyperactivity disorder (ADHD), remained virtually unchanged over the follow-up,[1] despite a relationship between epilepsy and psychiatric comorbidity has already been reported. Epilepsy-related variables, such as type and aetiology of epilepsy and frequency of seizures were likewise predictive of psychiatric comorbidity. The Kiddie Schedule for Affective Disorders and Schizophrenia for School-Age Children indicated a persistence at follow-up of the psychiatric conditions identified at baseline: this brings to mind the biological component of psychiatric comorbidity in epileptic patients.[1]

Celiac disease (CD) is a chronic, immune-mediated disorder, characterized by small intestinal malabsorption of nutrients after the ingestion of wheat gluten or related proteins from rye and barley, by genetically susceptible individuals expressing the HLA class II molecules DQ2 or DQ8, villus atrophy of the small intestinal mucosa, prompt clinical and histologic improvement following strict adherence to a gluten-free diet.[2] The overall prevalence of CD varies between 0.7% and 2% in the general population. The clinical manifestations of the disease vary greatly, and range from typical gastrointestinal manifestations (steatorrhea, vomiting, abdominal pain, diarrhea, muscle wasting, nutritional deficiencies) to absent, minimal, or unusual intestinal complaints with extraintestinal

manifestations or disorders (atypical CD).[2] Neurologic manifestations have been reported in about 6 to 10% of patients with CD. In particular, the more frequent described diseases have been cerebellar ataxia, peripheral neuropathy, migraine, autism, dementia, multifocal leukoencephalopathy and epilepsy. The clinical spectrum of epilepsy related to CD ranges from benign syndromes to intractable epilepsy with evolution to a severe encephalopathy, including progressive myoclonic epilepsy.[4] A more specific syndrome characterised by the association of CD, epilepsy, and occipital calcifications has also been reported, however this condition seems to be rare. Robust evidence of an association between temporal lobe epilepsy with hippocampal sclerosis and gluten sensitivity have been provided. The relative risk (RR) of developing epilepsy among children with CD is 2.1 (95% confidence interval [CI]: 1.5-2.8); the RR of CD among children with epilepsy is 1.7 (95% CI: 1.4-2.1). The precise mechanism of association between CD and epilepsy is unknown but several hypotheses have been proposed. It has been suggested that the antibodies associated with CD may be themselves neurotoxic or, alternatively, these may be a marker for a neurotoxic immunological process. Several authors have successfully demonstrated autoantibodies like anti-endomysium, anti-tissue transglutaminase and anti-reticulin in their cohort of epileptic patients.[3]

Children with CD are also at increased risk for mood disorders (RR, 1.2; 95% CI: 1.0-1.4), anxiety disorders (RR, 1.2; 95% CI: 1.0-1.4), ADHD (HR, 1.2; 95% CI: 1.0-1.4).[4] Psychiatric disorders occurring before the diagnosis of CD may be attributed to active CD, resulting in cerebral hypoperfusion, presence of proinflammatory cytokines, and low folate levels. However, the exact mechanisms underlying the association between CD and psychiatric disorders have yet to be established. The lack of increased risk of psychiatric disorders among healthy siblings of CD probands suggests an effect of CD *per se* rather than common genetic or within-family environmental factors. Before diagnosis, patients with CD often have a lower body mass index than the general population and often suffer from malnutrition. Several psychiatric disorders, including mood[5] and anxiety disorders,

and cognitive decline have been linked to malnutrition and vitamin deficiencies. Psychiatric morbidity in CD also may result from a chronic immune-mediated systemic reaction in CD.

Measurement of anti-tissue transglutaminase and anti-endomysium immunoglobulin A should be performed in patients with epilepsy and psychiatric comorbidity (antibody-positive patients should be offered a duodenal biopsy), as in the study by Gatta et al.[1] A gluten free diet in the diagnosed CD patients could have beneficial effects not only on seizures control but also in the management of the associated psychiatric disorders.

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